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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/634,320	08/09/2000	Mikhail I. Papisov	0838.1003-001	5525

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EXAMINER	
ZARA, JANE J	

ART UNIT	PAPER NUMBER
1635	

DATE MAILED: 04/07/2004

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No.	Applicant(s)	
	09/634,320	PAPISOV, MIKHAIL I.	
	Examiner	Art Unit	
	Jane Zara	1635	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *29 December 2003*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-96* is/are pending in the application.

4a) Of the above claim(s) *1-13,18,23-27,31-33 and 38-96* is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *14-17,20-22,28-30 and 34-37* is/are rejected.

7)☒ Claim(s) *19* is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449 or PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: _____.

DETAILED ACTION

This Office action is in response to the communication filed 12-29-03.

Election/Restriction

This application contains claims 1-13, 18, 23-27, 31-33, 35 and 38-96 drawn to an invention nonelected with traverse in Paper No. 13. A complete reply to the final rejection must include cancelation of nonelected claims or other appropriate action (37 CFR 1.144) See MPEP § 821.01.

Response to Arguments and Amendments

Withdrawn Rejections

Any rejections not repeated in this Office action are hereby withdrawn.

Maintained Rejections

Claims 14-16, 20-22 and 34 are rejected under 35 U.S.C. 102(b) as being anticipated by Warren for the reasons of record set forth in the Office action mailed 6-27-03.

Applicant's arguments filed 12-29-03 have been fully considered but they are not fully persuasive. Applicants argue that Warren does not qualify as prior art for the instant invention because Warren does not teach nucleotide drug carriers comprising non-covalently attached drugs. Applicant is correct and the 102 rejections for amended claims 36 and 37 have been withdrawn accordingly.

Applicants also argue that Warren does not qualify as prior art because there is no explicit teaching of the solubility concentrations of the drug-carriers comprising polynucleotides covalently attached to polymeric components, and applicant therefore concludes that the drug-carriers disclosed throughout the Warren reference do not possess an aqueous solubility of at least one mg/liter at 25°C. Contrary to Applicants' assertions, Warren teaches physiologically compatible drug carrier complexes for drug delivery to target tissues and target cells for treatment of various pathological conditions, including various neoplasia, dermatitis, alopecia areata, psoriasis, etc (see e.g. page 15 of Warren). The delivery systems disclosed by Warren, in order to deliver drugs in a physiological setting to intended target tissues and cells, must be physiologically compatible and hence soluble under physiological conditions. Absent evidence to the contrary, the drug carrier complexes comprise covalently associated nucleotides, polymers and drugs that are soluble under physiological conditions, including an aqueous solubility of at least one mg/liter at 25°C.

Claims 14-17, 20-22, 28-30, 34, 36 and 37 are rejected under 35 U.S.C. 103(a) as being unpatentable over Warren, Matysiak et al, Ishihara et al, Gao et al and Burke et al for the reasons of record set forth in the Office action mailed 6-27-03.

Applicant's arguments filed 12-29-03 have been fully considered but they are not fully persuasive. Applicants argue that, because of the deficiencies discussed above - with regard to non-covalent interactions between the nucleotide carrier and the drugs within the drug carrier complexes, and because of the lack of explicit solubility parameters in the teachings of Warren - the 103 rejection is improper because the

additional teachings of Matysiak et al, Ishihara et al, Gao et al and Burke do not remedy the deficiencies of Warren. Contrary to applicants' assertions, the delivery systems designed by Warren, in order to deliver drugs in a physiological setting, must be physiologically compatible and hence soluble under physiological conditions. Absent evidence to the contrary, the drug carrier complexes comprise covalently associated nucleotides, polymers and drugs that are soluble under physiological conditions, including an aqueous solubility of at least one mg/liter at 25°C.

Applicants suggest that the secondary references do not address the deficiencies of Warren, which deficiency in Warren is the requirement of covalent attachments between the nucleotide carrier and the drug in the drug delivery complex. Contrary to Applicants' assertions, Gao et al teach nucleotide-drug delivery complexes that are not covalently attached (see e.g. left column on page 2422 of Gao et al, where the nucleotide complexes are referred to as "noncovalent complexes" and complexes with a "reversible nature" that "enables the drug to dissociate from... the assembly."). Therefore, the deficiencies suggested in Warren are specifically addressed by the teachings of Gao.

Applicants also argue, on the one hand, that the instant specification refers to the nucleotide component of the carrier complex not as a drug (e.g. pages 22-23 of arguments filed 12-29-03), but as a carrier, and therefore the references relied upon in the instant 103 rejection do not qualify as prior art. On the other hand, applicants assert that the nucleotide component does act as a drug within the drug carrier complex (page 24 of arguments filed 12-29-03) The claimed invention, however, can encompass both

the nucleotide as a drug and as a carrier. The language of the claims does not provide any distinction, it recites drug-carriers and complexes and uses the terms *nucleotides* and *drugs* interchangeably. And, contrary to Applicant's assertions, the prior art cited in the instant rejection teaches nucleotide drug-carriers and complexes comprising nucleotides as either carriers (as Gao teaches) or as drugs (e.g. antisense; see Matysiak on pages 855, 857, 860; see Ishihara at col. 1; see also Burke at col. 3-7), including covalently and non-covalently attached nucleotides, and in the presence or absence of polymers (e.g. see col. 1 of Ishihara, describing nucleotide containing drug carrier-polymeric complexes; see also Burke col. 2 and 7). Therefore, the instant 103 rejection, relying on the combined teachings of Warren, Matysiak et al, Ishihara et al, Gao et al and Burke, render the instant invention obvious.

New Rejections

Claim Rejections - 35 USC § 112

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 14-17, 19-22, 28-30, 34-37 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

It is unclear what is meant by the term "double-stranded nucleotide" or "single-stranded nucleotide" (e.g. perhaps replacing "nucleotide" with –polynucleotide— or –sequence-- would be remedial).

In claim 14, lines 4-5, it is unclear whether the solubility of the polymer component refers to the polymer component alone, or after it is covalently attached to the polynucleotide portion of the carrier. Appropriate clarification is requested.

Allowable Subject Matter

Claim 19 appears free of the prior art or record.

Conclusion

Certain papers related to this application may be submitted to Art Unit 1635 by facsimile transmission. The faxing of such papers must conform with the notices published in the Official Gazette, 1156 OG 61 (November 16, 1993) and 1157 OG 94 (December 28, 1993) (see 37 C.F.R. § 1.6(d)). The official fax telephone number for the Group is **703-872-9306**. NOTE: If Applicant *does* submit a paper by fax, the original signed copy should be retained by applicant or applicant's representative. NO DUPLICATE COPIES SHOULD BE SUBMITTED so as to avoid the processing of duplicate papers in the Office.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to **Jane Zara** whose telephone number is **(571) 272-0765.** If attempts to reach the examiner by telephone are unsuccessful, the examiner's supervisor, John LeGuyader, can be reached on (571) 272-0760. Any inquiry regarding this application should be directed to the patent analyst, Katrina Turner, whose

telephone number is (571) 272-0564. Any inquiry of a general nature or relating to the status of this application should be directed to the Group receptionist whose telephone number is (703) 308-0196.

RAM R. SHUKLA, PH.D.
PRIMARY EXAMINER

JZ

4-1-04